

REMARKS

Status of the claims:

With the above amendments, claims 2, 3, 10, 11, and 13 are amended. Claims 2-13, 17-19, and 22-40 are pending and ready for further action on the merits. No new matter has been added by way of the above amendments. Support for the amendments can be found in original claim 12 and at page 5, first paragraph of the written description. Reconsideration is respectfully requested in light of the following remarks.

Rejections under 35 USC §102

Claims 2, 7, 9, 11, 17, 18, 19, 30, 31, 34, 35, and 38-40 are rejected under 35 USC §102(b) as allegedly being anticipated by Abad '740 (US Patent No. 5,538,740).

This rejection is traversed for the following reasons.

The Present Invention and Its Advantages

Claims 2 and 3, on which the outstanding Official Action is based has as component (b) at least one amino acid in pure form. For a person of ordinary skill in the art, the term "amino acid" means that the amino acid is present in pure form, that is, as a compound *per se* but not as an amino acid derivative. However, Applicants, in order to clearly express this issue in the claims, have amended claims 2 and 3 to recite "in pure form". The fact

that amino acids are added in pure form is further supported by amended claim 11 and by Examples 1 to 4. As was indicated in the response of March 10, 2003, the inventors of the present application found that the combination of amino acid(s) and zinc oxide and/or inorganic peroxides improves the microcirculation in the cell. The improvement can visually and biometrically be shown. If only salts are used, an increase in the microcirculation in the cell abruptly falls back to the starting value after about 1.5 hours. When the inventive composition comprising the combination of amino acid(s) and zinc oxide and/or inorganic peroxides is used, the improvement of microcirculation is greater, steadier, lasts longer and approaches the starting value slowly. This allows a better infiltration of agents such as secondary plant substances and better distribution of agents in the cell (see all of page 5 in the written description).

Furthermore, as was indicated in the response of March 10, 2003, a person of ordinary skill in the art of the present invention regards the term "secondary plant substance (SPS)" to mean a specific group of chemical compounds, that is, it comprises a specific group of substances in the same way as the term "vitamins" comprises a specific group of substances, the term "mineral salts" comprises a specific group of substances, the term "amino acids" comprises a specific group of substances and the like. SPS's are

used by the plants themselves. Plants produce these substances not in primary metabolism, but in secondary metabolism, which does not regulate the growth of the plant.

In the 1990's, people skilled in the art of nutrients determined that SPS's taken up by the food have benefits for the health. For example, if taken up with food, SPS's have anti-carcinogenic, anti-microbial, anti-oxidative and immunomodulating effects. Due to their chemical structure and functional properties, the SPS's can be subdivided into several groups as is claimed in claims 2 and 3. However, Applicants stress that it was generally not known to use SPS's in preparations for topical application. Applicant emphasizes that the effects of SPS's found in the art of nutrients generally are not transferred to the effects of preparations for topical application because the demands on such preparations are entirely different (for example, solubility considerations, etc).

Removal of the Rejection over Abad '740

Abad '740 describes a cosmetic composition comprising a filtrate of a secreted fluid from live gastropods. In Example III of Abad '740, it is indicated that the glandular secretions have been elementarily purified and fractionated by using a cation exchange resin. The principle groups of amino acids included are

described. Abad '740 discloses that the specifically prepared glandular secretion in this Example contained at least 8 amino acids and additionally allegedly atoxic substances (see column 9, lines 25 to 27 and 60). It should be noted that in this Example, the glandular secretions have been specifically treated for analysis. There is nothing in this example that clearly indicates that the amino acids found are present in the used glandular secretion in pure form. Particularly, there is no indication that in the liquid secretions used in the preparations such as creams, the active ingredient comprises any amino acid in pure form. In contrast, Abad '740 indicates in claim 1 and e.g. column 9, lines 23 to 28, that the glandular secretions comprise a multiplicity of amino acids and, in addition thereto, nontoxic substances, which are not further identified. However, contrary to the present invention, Abad '740 cannot provide a composition which comprises a specifically selected and desired amino acid or amino acids in pure form, that is, an amino acid without further substances of glandular secretions, which are not desired in the present invention. For example, Examples 1 to 4 of the present application contain specific amino acids in pure form in desired amounts. Such preparations are neither taught nor suggested by Abad '740.

Example XIV of Abad '740 describes a preparation of a deodorant cream comprising the excipient of Example IV comprising,

besides other ingredients, calcium carbonate and zinc oxide, active ingredients comprising glandular secretions, menthol and further ingredients. Applicant respectfully submits, as mentioned above, that the active ingredient of Abad '740 is not comparable with an amino acid in pure form, as is presently claimed because the active ingredient of Abad '740 always comprises a mixture of arbitrary amino acids in a not exactly disclosed form and further substances of the glandular secretions. Furthermore, menthol, although it is a terpene alcohol, is generally not regarded as a secondary plant substance. Applicant asserts that not every terpene is automatically a secondary plant substance. In particular, Applicant points to the text book of B. Watzl, C. Leitzmann, "Bioaktive Substanzen in Lebensmitteln (Bioactive Substances in Food)", Hippokrates Verlag Stuttgart (1995), (copy of section attached), which indicates that the term "secondary plant product" is well known (see page 4, left column at the marked passage of the enclosed copies). Bioactive substances in food are subdivided into three groups, namely secondary plant substances, dietary fibers, and substances in fermented food (see page 7, right column, 3rd paragraph and page 9, right column, first table).

It should be noted further that in the United States, the health supporting effect of secondary plant substances are investigated intensively. At the University of Illinois in Chicago

a specific database has been arranged comprising over 50,000 references regarding the health supporting effect of secondary plant substances. Furthermore, the National Cancer Institute in the United States supports a 5-year program regarding the investigation of anti-carcinogenic effects of secondary plant substances (see page 8, left column, second paragraph). That is, as was indicated in the response of March 10, 2003, the term "secondary plant substance" is well known to a person of ordinary skill in the art.

Applicant, however, emphasizes that the textbook of Watzl and Leitzmann is not relevant for the present invention because it exclusively relates to bioactive substances in food. Contrary thereto, the present invention relates to compositions for topical administration. Applicant stresses further that there is nothing in this text book that makes it obvious to or which motivates a person of ordinary skill in the art to incorporate secondary plant substances into preparations for topical administration. There is nothing in this reference which makes it obvious whether the group of secondary plant substances incorporated in preparations for topical administration are pharmaceutically active or even effective at all.

The incorporation of amino acids in pure form, particularly in combination with a salt and zinc oxide and/or an inorganic peroxide

is not suggested by Abad '740. Furthermore, there is nothing in Abad '740 about the specific effects and advantages of such a specific combination as disclosed at e.g. page 5 of the application. Thus, as argued above, Abad '740 cannot anticipate the instant invention nor can it render obvious the instant invention because Abad '740 fails to disclose the elements of the instantly claimed invention. Withdrawal of the rejection is warranted and respectfully requested.

Rejections under 35 USC §103

Claims 2-9, 11, 13, 17-19, 22-35, and 38-40 are rejected under 35 USC §103(a) as allegedly being unpatentable over Herish '791 (US Patent No. 5,667,791).

Claims 2, 6, 7, 9-12, 17-19, 28-31, and 34-40 are rejected under 35 USC §103(a) as allegedly being unpatentable over Hillebrand '500 (US Patent No. 5,296,500).

Present Invention

The present invention, as recited in claim 1, relates to a preparation for topical application comprising the following components:

(a) at least one salt selected from alkali metal salts, alkaline earth metal salts and other minerals,

(b) at least one amino acid in pure form,

- (c) zinc oxide and/or an inorganic peroxide, and
- (d) at least one secondary plant substance selected from the group consisting of carotinoids, phytosterols, saponins, polyphenols, flavonoids, terpenes, phytoestrogens, sulfides, phytin acid, dietary fibers and combinations thereof.

Disclosure of Hersh '791

Hersh '791 discloses a composition of glutathione and a selenoamino acid in a topical carrier and a method of using the composition to reduce and repair x-ray radiation-induced skin damage.

Disclosure of Hillebrand '500

Hillebrand '500 discloses a method for regulating wrinkles and/or atrophy in mammalian skin comprising treating the skin with a safe and effective amount of N-acetyl-L-cysteine and/or a derivative thereof.

Removal of the Rejection over Hersh '791

Hersh '791 describes a composition for topical application comprising L-selenomethionine and glutathione. This composition may further comprise green tea, superoxide dismutase and a zinc salt (see claims 1, 4, 6 and 10). The disclosure of Hersh '791 is that

glutathione in combination with a selenoamino acid, used topically, acts as free radical scavenger reducing radiation-induced skin changes (see column 2, last paragraph to column 3, line 41). As confirmed by the Examiner, there is no working example in Hersh '791 which uses zinc oxide. However, amended claims 2 and 3 require at least one amino acid in pure form. Selenomethionine is regarded as an amino acid derivative which is not an amino acid in pure form as required by the claims. Therefore, the new set of claims is novel over Hersh '791. As mentioned above, Hersh '791 is based on the teaching that a combination of glutathione and selenomethionine reduce x-ray radiation-induced skin damage. Hersh '791 does not teach or suggest any composition comprising an amino acid in pure form.

Furthermore, Hersh '791 neither discloses nor suggests a composition comprising a combination of amino acids in pure form with zinc oxide and/or an organic peroxide. Moreover, there is nothing in Hersh '791 pointing to a specific combination of an amino acid in pure form, zinc oxide and a SPS. As mentioned above, the present invention is based on the finding that a combination of amino acid(s) with zinc oxide and/or inorganic peroxide improves the microcirculation of the cell. This allows a better infiltration of agents such as SPS and a better distribution of such an agent in the cell. The teaching of Hersh '791 is contrary

thereto. There is nothing in Hersh '791 which makes obvious a preparation according to amended claims 2 and 3 to a person of ordinary skill in the art nor any of the effects thereof.

The Examiner, furthermore, indicated that the artisan of ordinary skill would be motivated to add zinc oxide into Hersh '791's therapeutic compositions. Applicant respectfully disagrees. It should be stressed that, although Hersh '791 describes in column 9, 3rd paragraph that zinc oxide has healing properties on wounds, the examples of Hersh '791 do not use zinc oxide. This is a further indication that there is nothing in Hersh '791 pointing to a combination of an amino acid with zinc oxide. Therefore, because Hersh '791 does not disclose the elements of the instant claims, Hersh '791 cannot render obvious the instant invention. The rejection is inapposite. Withdrawal of the rejection is warranted and respectfully requested.

Removal of the Rejection over Hillebrand '500

Hillebrand '500 describes a method for regulating wrinkles or atrophy in mammalian skin using a composition comprising N-acetyl-L-cysteine or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier. The teaching of Hillebrand '500 is to use N-acetyl-L-cysteine or a pharmaceutically acceptable salt thereof for regulating wrinkles (see column 1,

penultimate paragraph). In the section entitled "Zinc Salts" from column 3, last paragraph to column 5, 1st paragraph, Hillebrand '500 indicates that the compositions are rendered substantially odorless by adding a zinc salt. The zinc most likely removes odors by complexing with malodorous H_2S , which may be formed in trace amounts as the active compound decomposes (see column 3, lines 56 to 62). Similar to Hersch '791, Hillebrand '500 does not describe any composition comprising an amino acid in pure form. N-acetyl-L-cysteine is an amino acid derivative. Furthermore, Hillebrand '500 does not teach a combination of an amino acid in pure form and zinc oxide and/or inorganic peroxide. In column 7, penultimate paragraph of Hillebrand '500, there is a list of compounds disclosed, with "soybean saponins" being one in this list with a multiplicity of other compounds. Nothing in Hillebrand '500 points particularly to the group of secondary plant substances. Moreover, nothing in Hillebrand '500 points to any improving effects of a composition comprising an amino acid in pure form, zinc oxide and/or inorganic peroxide acid SPS. Further, there is no hint in Hillebrand '500 that by the specific combination of components of the present invention health improving substances, particularly SPS's, can be infiltrated better into the cell. Applicant submits there is no motivation for a person of ordinary skill in the art to replace the amino acid derivative in an example

of Hillebrand '500 by any amino acid in pure form and, in addition thereto, add SPS in a pharmaceutically effective amount. It is absolutely incorrect, as alleged by the Examiner, that the skilled artisan would have a reasonable expectation of success by doing this since Hillebrand '500 is absolutely silent concerning any effects of a combination of amino acid, zinc oxide and SPS. Therefore, Hillebrand '500 cannot render obvious the instant invention because Hillebrand '500 fails to disclose the elements of the instant invention. Withdrawal of the rejection is warranted and respectfully requested.

Conclusion

Applicants submit that the Examiner is using hindsight reconstruction to arrive at the instant invention. Only knowledge in advance of the presently claimed invention could lead one of skill in the art to the combination that is taught in the instant invention. However, to "imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art references or record convey or suggest that knowledge is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taut is used against its teacher." *W.L. Gore & Assoc. v. Garlock, Inc.* 220 USPQ 303, 311 (Fed. Cir., 1983).

With the above remarks and amendments, it is believed that the claims, as they now stand, define patentable subject matter such that passage of the instant invention to allowance is warranted. A Notice to that effect is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact T. Benjamin Schroeder (Reg. No. 50,990), at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachments: B. Watzl, C. Leitzmann, "Bioaktive Substanzen in Lebensmitteln (Bioactive Substances in Food)", Hippokrates Verlag Stuttgart (1995)